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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,106	10/09/2006	Morris J. Robins	49506-7	1963
26582	7590	10/04/2007		
HOLLAND & HART, LLP P.O BOX 8749 DENVER, CO 80201			EXAMINER LAU, JONATHAN S	
			ART UNIT 1609	PAPER NUMBER
			MAIL DATE 10/04/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,106	ROBINS ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☒ Claim(s) 1,3 and 5 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1</u> page. | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

This application is the national stage entry of PCT/US03/30386, filed 25 Sept 2003, and claims benefit of US Provisional Application 60/413,915, filed 25 Sept 2002, and US Provisional Application 60/416,329, filed 04 Oct 2002. Claims 1-6 are currently pending and are examined on the merits herein.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if

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the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The disclosure is objected to because of the following informalities:

as recited above, the section headings should appear in upper case, without underlining or bold type. In the instant application the sections headings appear to be in upper case, but with underlining and possibly bold type, and

the presence of minor spelling and typographical errors such as:

Page 1, line 10, "deaminase-resistant" is misspelled,

Page 3, line 8, "replace the 2-amino group with a 6-chloro group" may intend to mean "replace the 2-amino group with a 2-chloro group".

Page 6, line 18, "nucloside" is misspelled.

Appropriate correction is required.

Claim Objections

Claims 1, 3, and 5 are objected to because of the following informalities: minor spelling errors such as:

In claim 1, step (b), "diazotization/chloro-dedi[a]azoniation",

In claim 3, step (a), "cycloalkyl", and

In claim 5, step (a), "diazotization/chloro-dediavoniation".

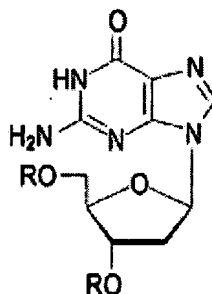
Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 5 has been amended to be drawn to a "method for producing 2-chloro-2'-deoxyadenosine comprising the steps of: (a) converting the 6-oxo



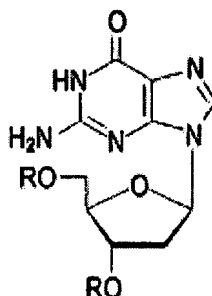
group of a compound having the formula

... into a 6-leaving group

having greater reactivity than that of the 2-amino group in a diazotization/chloro-dediazoniation [sic] displacement reaction". In the preliminary amendment filed 25 Mar 2005 Applicant argues that the basis for this amendment is found in the specification, page 5, lines 5-7. However, this section of the specification as amended recites "transformation of the 2-amino function to a 2-chloro functional group by diazotization/chloro-dediazoniation of the 2-amino function, and selective C6

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ammonolysis of the 2-chloro-6-(substituted)purine derivatives, with accompanying sugar deprotection." The only reference to the reactivity at the C6 position of the purine to diazotization/chloro-dediazoniation may be found in the specification on page 9, lines 2-4, "These procedures provide efficient diazotization/halo-dediazoniation of protected (2 or 6)-aminopurine nucleosides as well as the acid-sensitive 2'- deoxynucleosides." However, this section does not provide support for the claim of "converting the 6-oxo



group of a compound having the formula ... into a 6-leaving group having greater reactivity than that of the 2-amino group in a diazotization/chloro-dediazoniation [sic] displacement reaction".

Claim Rejections - 35 USC § 112

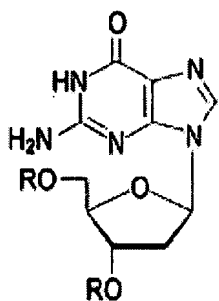
The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 5 recites "A method for producing 2-chloro-2'-deoxyadenosine comprising the steps of: (a) converting the 6-oxo group of a compound having the formula



wherein R is a protecting group selected from the group consisting of acetyl, benzoyl, into a 6-leaving group having greater reactivity than that of the 2-amino group in a diazotization/chloro-dediazoniation [sic] displacement reaction; (b) replacing the 2-amino group with a 2-chloro group by diazotization/chloro-dediazoniation of the 2-amino group; (c) replacing the 6-leaving group with a 6-amino group by selective ammonolysis of the 6-leaving group; and (d) removing the R protecting groups by deacylation, to produce 2-chloro-2'-deoxyadenosine."

As claimed, the 6-leaving group has greater reactivity than that of the 2-amino group in a diazotization/chloro-dediazotization displacement reaction, which is performed in step (b) replacing the 2-amino group with a 2-chloro group by diazotization/chloro-dediazotization, a diazotization/chloro-dediazotization displacement reaction. Claim 5 then recites that the 6-leaving group remains after the diazotization/chloro-dediazotization displacement reaction in the subsequent step, "(c) replacing the 6-leaving group with a 6-amino group by selective ammonolysis of the 6-leaving group". It is vague and indefinite what the claimed 6-leaving group is that has a greater reactivity than the 2-amino group in a diazotization/chloro-dediazotization

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displacement reaction but does not react along with the 2-amino group in the a diazotization/chloro-dediazotization displacement reaction claimed in step (b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

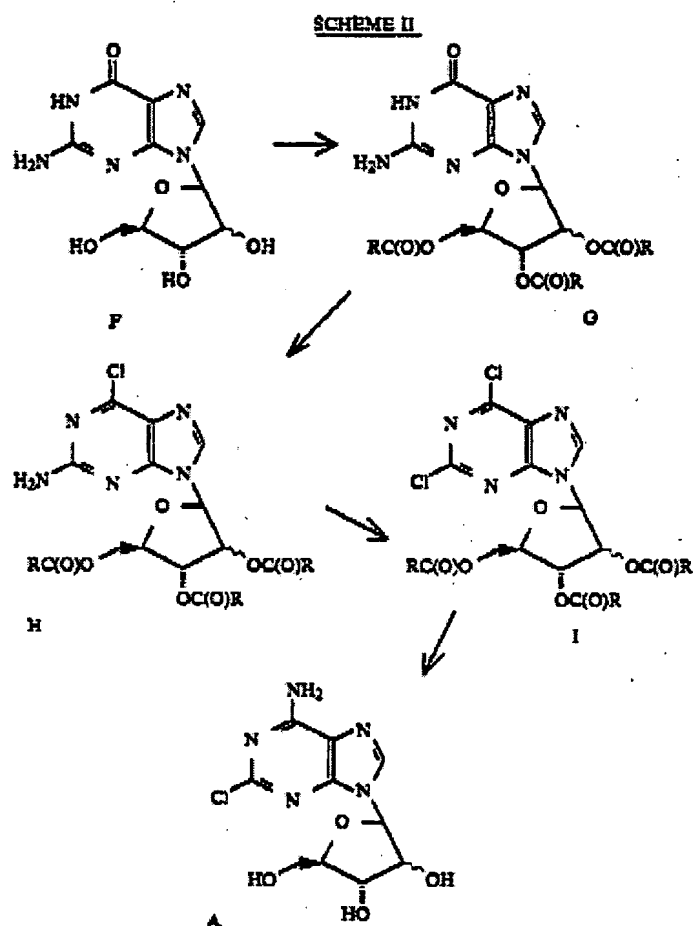
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (US Patent 5,208,327, cited in PTO-892).

Chen discloses the reaction of guanosine wherein the hydroxyl groups of the sugar are protected with acetyl groups (see chemical structure column 2, lines 1-13) to give 2-chloroadenosine comprising the steps of reacting the 6-oxo group with an inorganic acid chloride to give the 6-chloro compound, replacing the 2-amino group with

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a 2-chloro group by a diazotization/chloro-dediazotization reaction using a nitrosylating agent such as an alkyl nitrite and a chloride source such as an alkyl chloride, and replacing the 6-chloro group with a 6-amino group and removing the R protecting groups as per scheme II (column 6 lines 5-42):



See Chen, column 6 lines 56-58, 61-64, and 67. Chen discloses the conversion of the 2-chloroadenosine to the 2-chloro-2'-deoxyadenosine after conversion of the guanine moiety to a 2-chloroadenine moiety.

Chen does not disclose the conversion of 2'-deoxyguanosine to 2-chloro-2'-deoxyadenosine.

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It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of converting the guanine moiety to a 2-chloroadenine moiety disclosed by Chen with 2'-deoxyguanosine in place of guanosine. Chen teaches that the conversion of the guanine moiety to a 2-chloroadenine moiety may be practiced with an analog or derivative of guanosine, in particular analogs with variation at the 2' position. See Chen, column 6, lines 2-3 and 46-47. It would have been obvious to one of ordinary skill in the art at the time of the invention that it would have been simple substitution of one known element for another to obtain predictable results to practice the invention of Chen with 2'-deoxyguanosine in place of guanosine, such as by changing the sequence of adding ingredients to generate 2'-deoxyguanosine first and then converting the 2'-deoxyguanosine to 2-chloro-2'-deoxyadenosine. Both the method disclosed by Chen and the method claimed in the instant application produce the same end product, 2-chloro-2'-deoxyadenosine. Both the method disclosed by Chen and the method claimed in the instant application comprise reactions at the guanine moiety, with protecting groups affixed to the sugar moiety so that it does not react.

Claims 3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (US Patent 5,208,327, cited in PTO-892) as applied to claims 1, 2 and 4 above, and further in view of Bauman et al. (US Patent 5,668,270, cited in PTO-892).

As recited above, Chen discloses the reaction of guanosine wherein the hydroxyl groups of the sugar are protected with acetyl groups (see chemical structure column 2,

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lines 1-13) to give 2-chloroadenosine with an intermediate reaction of the 6-oxo group to a 6-chloro group followed by the conversion of the 2-chloroadenosine to the 2-chloro-2'-deoxyadenosine.

Chen does not disclose the conversion of the 6-oxo group to a 6-leaving group wherein the 6-leaving group is a 6-O-sulfonyl leaving group.

Bauman et al. teaches the conversion of the 6-oxo group of guanosine to a 6-amino group with an intermediate reaction of the 6-oxo group of guanosine with a 6-O-sulfonyl leaving group, where the sulfonyl group is an alkyl or aryl sulfonyl group, in the place of the 6-halo group. See Bauman et al. column 3, lines 36-49.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of converting the guanine moiety to a 2-chloroadenine moiety disclosed by Chen with a 6-leaving group is a 6-O-sulfonyl leaving group in the place of a 6-halo leaving group. It would have been simple substitution of one known element for another to obtain predictable results to practice the invention of Chen with a 6-O-sulfonyl leaving group in the place of the 6-halo leaving group as taught by Bauman. The methods in both references involve a similar reaction, 2-halo-adenosine produced from guanosine. Both methods comprise reactions at the 6-oxo group of a purine moiety.

Conclusion

No claims are found to be allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Ardin Marschel can be reached on 571-272-0718 or Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSL

 10/11/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER